28

EXHIBIT 28

AMERICAN ACADEMY OF ALLERGY ASTHMA & IMMUNOLOGY

ACAAI American College of Allergy, Asthma & Immunology

Follow the Leader Into the Future

August 31, 2004

Dear Colleague,

We are writing to bring to your attention a coalition of interested individuals in the allergy, pulmonary, pediatric, pharmaceutical, and lay organization communities that has been formed to address the growing problem of substandard pharmacy compounding of respiratory medications for nebulization. It is called Consumer Health Alliance for Safe Medication (CHASM). With this coalition, we will pool our resources to get the FDA to oversee pharmaceutical compounding of respiratory medications. We're aware of pharmacies making budesonide and albuterol combinations, budesonide and ipratropium combinations, and combinations of all three for nebulization. There are no data to support the efficacy of these combinations in outpatient settings nor to assure their chemical compatibility in solution. Poorly manufactured respiratory agents could result in increased drug-related morbidity and mortality for our asthma patients. This could occur from:

- Toxicity from super-potency
- Failed responses to therapy due to sub-potency
- Infection from bacterial or fungal contamination
- Respiratory complications from intolerable levels of endotoxin or other adulterants

There can be a major liability problem for allergists. If you authorize a substitution for nebulization medications and your patient is injured, it is you, the allergist, that is liable -- not the pharmacists who do not have any responsibility to disclose risks, to assure safety, etc.

CHASM believes that, in making its case to the FDA, it would be important to obtain letters from physicians who had been fooled by the pharmacists about substitution with compounded respiratory medications, or worse, had a patient who was injured as a result. If this has happened to you, please report it to:

David Horowitz, JD
Director, Office of Compliance
Center for Drug Evaluation and Research (CDER)
Food and Drug Administration
11919 Rockville Pike
Room 405
Rockville, MD 20852

Please be sure to copy the AAAAI or the ACAAI Executive Office on any letters you do send. All of us in the allergy community are very concerned about the welfare of our patients. We must work to ensure our patients receive effective and safe medications.

Sincerely,

Michael S Schatz, MD

Michael Schatz, MD, MS
FAAAAI
AAAAI President

Michael Blaiss, MD
ACAAI President

[redacted] [redacted]

FROM ACAAI MONTHLY e-NEWS TO MEMBERS

A Message from ACAAI President Michael Blaiss, MD:

The next issue I want to bring to your attention is substandard pharmacy compounding of respiratory medications for nebulization. We usually think of pharmacy compounding as taking pills and making them into a liquid form for children or producing designer creams or ointments for atopic dermatitis by mixing different topical agents. But recently pharmacy compounding has moved into the realm of unregulated drug manufacturing with the possibility of producing substandard products. It is extremely profitable for the compounding pharmacists. I'm aware of pharmacies making budesonide and albuterol combinations, budesonide and ipratropium combinations, and combinations of all three for nebulization. Poorly manufactured respiratory agents could result in increased drug related morbidity and mortality for our asthma patients. This could occur from:

- toxicity from super potency
- failed responses to therapy due to subpotency
- infection from bacterial or fungal contamination
- respiratory complications from intolerable levels of endotoxin or other adulterants

Here are some examples of the serious consequences from compounding respiratory agents for nebulization. In 2001, Med-Mart Pharmacy, of Novato, Calif., distributed more than 4,000 doses of compounded respiratory drugs contaminated with serratia bacteria. An investigation by the California Board of Pharmacy and the FDA found the pharmacy did not have proper training, equipment or control procedures in place to ensure the quality of dosage forms produced, and the testing of finished drug products was inadequate to ensure potency, purity and sterility. A subsequent Warning Letter issued to Med-Mart by the FDA noted the agency's serious concern about the public health risks associated with "large-scale production of massive quantities of inhalation solutions without these products being required to meet all the laws and regulations applicable to a drug manufacturer." The Warning Letter further noted that, despite knowledge of the original contamination, the pharmacy failed to prevent further adulteration of another lot of drug that was found to be contaminated with the bacteria Bacillus megaterium.

In July 2002, two Florida pharmacists were convicted of Medicare fraud for their role in the large-scale compounding of adulterated respiratory medications by unlicensed individuals under unsanitary conditions. During the trial, testimony from an expert witness for the defense highlighted larger respiratory compounding operations throughout the United States, suggesting the invasive nature of this practice.

In March 2003, more than 4,000 liters of purportedly sterile, compounded respiratory solutions contaminated with Pseudomonas cepacia were distributed to an estimated 18,000 vulnerable respiratory patients throughout the United States. Independent Med-4-Home Pharmacy, of Kansas City, Mo., compounding drugs on behalf of national homecare company, Lincare, refused to cooperate with a recall and did not alert patients or prescribers to the contamination. Though the FDA noted that there were no reported injuries in the Med-4-Home case, there was limited surveillance and no follow-up investigation of exposed cases to assess for morbidity or mortality.

The above information was provided by The Respiratory Care Board of California and Sarah Sellers, PharmD, who is working with the Allergy and Asthma Network/Mothers of Asthmatics on this issue. In fact, there will be a hearing in the near future on Capitol Hill about this major medical problem, as the FDA is looking at

taking steps to regain authority to regulate pharmacy compounding. Of course, the compounding pharmacists and their lobbying organization are fighting any changes. The College will work with AANMA and others on this important issue for our patients.

What can you do now? Here are some suggestions from The Respiratory Care Board of California.

• Review the FDA Compliance Policy Guide Sec.460.200 Pharmacy Compounding.

• Be alert to the potential for unapproved, substandard compound drugs to enter drug supply chains without appropriate authorization

• Report any medication-related adverse reactions, including failed therapies, to the FDA MedWatch program, state boards of pharmacy and state boards of health.

• Be aware that medically necessary compounded drug products should be filled on a per-prescription basis and should include a complete disclosure of risk to the patient.

I believe that if there is any question about your patient's respiratory medication for nebulization, please have it brought to your office for verification. Nothing is more important than our patient's safety.

Michael S. Blaiss, M.D.

Respiratory Update

September 2003

New Continuing Education Requirements

The Board has been working with you to strengthen our continuing education (CE) guidelines and is pleased to report the new regulations will go into effect November 1, 2003. All CE acquired on or after November 1st, must meet the new criteria.

The new guidelines continue to require a total of 15 hours of CE every two years with a minimum of 2/3 (10 hours) being directly related to clinical practice [the other 1/3 (5 hours) may be related to the general practice of respiratory care]. The most significant changes now require courses to be approved or provided by recognized entities and limit the credit granted for repeating examinations and courses in connection with credentials and certifications as noted on page 14

Recognizing Men and Women in Uniform, Board Requests Your Aid

It was only earlier this year when our sons, daughters, mothers, fathers and friends were called upon to protect our country and further our fight against one of the greatest threats our country has ever faced. Terrorism. And they responded. Our men and women in uniform honored their commitment to protect and serve our country

More than 300,000 troops were deployed to the Middle East as part of Operation Iraqi Freedom. Thousands of reserves were called upon to enter into active combat or assume duties on our homeland for the others who went into battle. There is no question that all Americans continue to stand united in support of our troops.

The major combat operations in Iraq were declared over shortly after Iraqi civilians, with assistance from U.S. troops and an armored vehicle, toppled a statue of Hussein on April 9th. Yet our Marines and soldiers continue to be targets of hostile attacks. Since March 20th, when the battles began, over 260 US troops have died while defending our country.

We are all sincerely grateful for every person in uniform who has defended or is defending our country this year in the Middle East. The Board would like to recognize and honor every California respiratory therapist who served or is serving our country in this war, whether the therapist is a full-time service man/woman or a reservist, who was deployed to the Middle East or called to duty to oversee homeland operations during these trying times.

If you or someone you know fits this description, please contact Stephanie Nunez, Executive Officer as soon as possible and let her know the therapist's name and contact information (or your contact information). You can call Ms. Nunez at (866) 375-0386 or send her an e-mail: rcbinfo@dca.ca.gov. The Board would like to make a very special presentation to these courageous service men and women

November Board Meeting

LOCATION CHANGE

Please note the venue for the Board's November 14th meeting, originally scheduled to be held in San Diego has been changed. Due to fiscal restraints affecting all State agencies, the Board's November 14th meeting will be held in Sacramento.

Please watch our website for the most up-to-date information. The agenda for this meeting will be available after November 4th, on the Board's website: www.rcb.ca.gov

All Board meetings are open to the public

Inside This Issue

Published by the Respiratory Care Board of California 444 North 3rd Street, Suite 270, Sacramento, CA 95814
Telephone (916) 323-9983 Toll-Free (866) 375-0386 Fax (916) 323-9999 E-Mail: rcbinfo@dca.ca.gov Web: www.rcb.ca.gov

The Center for the Health Professions Takes Notice

The Center for the Health Professions (The Center) released a new publication in July addressing the respiratory care profession. The 8 page document touches on all aspects of the profession: the current challenges the profession is facing, including workforce shortages and potential solutions. The Board, the AARC, and Rick Ford, RCP, as well as a handful of others were interviewed and cited as sources for the publication.

To review the complete 8-page paper, please visit The Center's website at www.futurehealthprofessions.com

If you know anyone interested in learning more about a career in the respiratory care field, please have them visit our website or contact the Board's toll-free line for a free career brochure.

Website: www.rcbtx.org Toll-free: (866) 375-0386 E-Mail: rcb@rcbtx.org

Pharmacy Compounding

Pharmacy compounding has historically involved the manipulation of FDA-approved drug products into alternative dosage forms to meet the unique needs of individual patients. For instance, the compounding of tablets into a liquid dosage form for a pediatric patient is often medically necessary and indeed legitimate. But increasingly, pharmacy compounding is moving into the realms of unregulated drug manufacturing, with the potential to expose large populations to substandard drug products. This emerging, contemporary compounding industry has manufactured, marketed and distributed large quantities of drugs in the absence of confirmed potency, purity, or sterility—and in many cases without full, knowledgeable and express consent of physicians and patients.

Benefits and Risks

Compounding serves a valuable professional role in cases where no dosage forms exist to meet a patient's specific needs and expected benefits outweigh anticipated and unanticipated risks. In some cases, however, financial benefits to pharmacies and providers may be the primary determinant of compounding, exposing patients to unnecessary and unacceptable risks.

Considered tip of the iceberg by public health officials, recently publicized cases throughout the US involving the large scale, substandard compounding of respiratory drugs raises concern...

Poorly manufactured, unregulated respiratory drugs represent a serious public health concern as they may result in increased drug-related morbidity and mortality. Patients may inadvertently experience:

- Toxicity from super-potency
- Failed responses to therapy from sub-potency
- Infection from bacterial or fungal contamination
- Respiratory complications from intolerable levels of endotoxins or other adulterants

Such concerns have been heightened by a recent FDA survey which found a 34% failure rate for compounded drugs evaluated for potency and purity (1). Throughout the country, compounded medications have been associated with deaths from meningitis, cases of paralysis, hospitalizations from toxic overdoses, exposures to contaminated drug products, and disease exacerbation due to dangerously sub-potent medications. Alarmingly, there are no current requirements to report adverse events associated with compounded drugs—nonetheless, known cases of injuries and deaths have surfaced gaining broad attention (2, 3).

How widespread is the problem? We really do not know, but public health experts are concerned. The CDC recently recommended that physicians consider exposure to substandard, compounded drugs for unexplained sources of infection following spinal or intra-articular injections (4). CDC further cautioned that health systems may not even realize they are purchasing compounded drugs (4), mandating diligence and caution in drug purchasing procedures to minimize the inadvertent acquisition of substandard products.

Respiratory Compounding Industry

Considered tip of the iceberg by public health officials, recently publicized cases throughout the US involving the large scale, substandard compounding of respiratory drugs raises concern

Case 1 In 2001, Med-Mart pharmacy, located in Novato, California issued a Class I recall of thousands of doses of compounded respiratory medications distributed to managed care patients that were discovered to be contaminated with

Continued on Page 9

serratia liquiformins. A subsequent Warning Letter issued to Med-Mart by the FDA noted the agency's serious concern about the public health risks associated with "large-scale production of massive quantities of inhalation solutions without these products being required to meet all the laws and regulations applicable to a drug manufacturer" (5). After a joint inspection with the California Board of Pharmacy and the FDA found the pharmacy did not have proper training, equipment or control procedures in place to ensure the quality of dosage forms produced and testing of finished drug products was inadequate to ensure potency, purity and sterility, the pharmacy's next lot of drug produced, after the Serratia liquifaciens contaminated lots were detected, contained another contaminant, Bacillus megaterium (5).

Case 2 Two Florida pharmacists were convicted of Medicare fraud in July of 2002 for their role in the large scale compounding of adulterated respiratory medications by unlicensed individuals under unsanitary conditions. During the trial, testimony from an expert witness for the defense highlighted larger respiratory compounding operations throughout the US, suggesting the invasive nature of this practice.

Case 3: Med-4-Home Pharmacy in Kansas City, Missouri recently distributed more than 1.3 million doses of compounded albuterol and ipratropium solution for nebulization to an estimated 18,000 patients nationwide—the purportedly sterile drugs were contaminated with Pseudomonas cepacia (6) The Missouri State Board of Pharmacy found Med-4-Home failed to completely recall the distributed medication and did not adequately inform physicians and patients of the contamination risk (6)

Current Legal Framework

In April of 2002, the US Supreme Court struck down provisions in Federal law that had provided FDA oversight of pharmacy compounding, leaving primary regulatory enforcement with state boards of pharmacy. However, state compounding regulations are discrepant and in some cases nonexistent—today's patchwork of state laws provides little protection to unsuspecting patients who typically believe all drug products are safe, effective and well regulated by the FDA.

In California, the state Board of Pharmacy recently introduced new sterile compounding regulations in response to deaths from contaminated spinal injections; however, the new regulations, though offering some public health protections for parenteral products, do not apply to the compounding of sterile respiratory drugs

Policy Initiatives

Recognizing the real and growing danger to patient safety posed by unregulated, compounded drugs, the FDA has expressed concerns that current law is insufficient to adequately protect public health and safety. According to Jane Axelrad, Associate Director for Policy at the FDA's Center for Drug Evaluation and Research, the Agency plans to issue a new draft guidance on compounding for comment, and that the FDA may seek new legislation to regain statutory authority to regulate pharmacy compounding. In addition, congressional interest and concern is growing in both houses.

What Clinicians Can Do

- Review the FDA's Compliance Policy Guide Sec. 460.200 Pharmacy Compounding, at: http://www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg460-200.html
- Recognize that financial incentives and convenience are inappropriate reasons to compound respiratory drugs
- Be alert to the potential for unapproved, substandard compounded drugs to enter drug supply chains without appropriate authorization
- Report any medication-related adverse events, including failed therapies, to the FDA's ModWatch program, state boards of pharmacy and state boards of health.
- Be aware that medically necessary compounded drug products should be filled pursuant to a unsolicited prescriber's request, on a per-prescription basis and should include complete disclosure of risk to patients.

More Information

For more information on this issue, please contact Sarah Sellers, Pharm D, The Center for Pharmaceutical Safety at (847) 207-0216 or E-Mail: ssellers@jhsph.edu.

Notes

1 Subramaniam V, Sokol G and Zenger V et al Survey of drug products compounded by a group of community pharmacies Findings from a Food and Drug Administration study. Available at http://fda.gov/cder/pharmcomp/communityPharmacy/default.htm

2 Russell S and Hallissy E Chronicle Investigation Who's mixing your drugs? Bad medicine Pharmacy mix-ups a recipe for disaster *San Francisco Chronicle* June 23 2002 Available at http://www.sfgate.com/cgi-bin/article.cgi?file=/chronicle/archive/2002/06/23/MN122273.DTL

3 Morris M and McGuire D Rx for disaster Some pharmacists who mix medicines dispense unsafe drugs *The Kansas City Star* October 6-8 2002

4 From the Centers for Disease Control *Exophiala* infection from contaminated injectable steroids prepared by a compounding pharmacy—United States, July—November 2002 MMWR December 13 2002/51(49) 1109-1112 Available at www.cdc.gov/mmwr/preview/mmwrhtml/mm5149a1.htm

5 FDA warning letter to Med-Mart Pulmonary Services available at http://fda.gov/foi/warning_letters/g3527d.htm

6 Harlow S Missouri officials begin tracking contaminated drug *The Kansas City Star* March 13, 2003

Recalls of Bulk Chemicals for use in Pharmacy Compounding

The quality of bulk actives used in compounding is suspect; pharmacists generally do not have the ability to test chemicals for identity, potency, purity and/or contamination. The recalls noted below are not comprehensive; surveillance of ingredients used in compounding is limited.

April 2003 Medisca Pharmaceutique: Norfloxacin 25 gram bottles. Product contained wrong drug, grepafloxacin, a drug removed from the market for safety reasons (severe renal and liver damage).

August 2000 Hawkins Chemical: Chloroquine Phosphate; 5,200 grams shipped to 9 states packaged 2/99. Product contained wrong drug (clonidine, a potent antihypertensive drug-if used in doses consistent with chloroquine oral dosing-life threatening toxicity would likely result).

January 2000 Spectrum Laboratory: Dihydroergotamine mesylate; unknown quantity shipped to 8 states. Product potentially contaminated with cephalosporin antibiotic.

January 2000 Meridian Pharmaceuticals: 23 active and inactive ingredients recalled due to potential contamination with penicillin or cephalosporin antibiotic; total of 340 containers distributed nationwide.

February 2000 Paddock Laboratories: Testosterone 1,000 bottles (5 gm) distributed nationwide. Some units contained wrong drug (testosterone propionate).

January 2000 Abbott Laboratories: Cyclosporin; 57.76 kg distributed to 5 states. Product failed impurity (residual solvent) level.

April 1999 Medisca, Inc: Liothyronine Sodium; 3,271 mg shipped to 13 states package date unknown. Product contained wrong drug (levothyroxine).

January 1998 Paddock Laboratories: Polymyxin B Sulfate; 269.5 gm to 8 states. Product contained wrong strength.

May 1995 Paddock Laboratories: Hydrocortisone, micronized; 1,927 bottles (25 gm) distributed nationally. Product contained the wrong amount of drug.

August 1992 Professional Compounding Centers of America: Albuterol Sulfate; 8.945 gm distributed nationally. Product contained wrong drug (dextromethorphan hydrobromide).

Sellers updated 6/13/03